UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,600	10/28/2003	Dennis A. Steindler	7203-8	6329

7590 09/06/2007

Stanley A. Kim, Ph.D., Esq.
Akerman Senterfitt
Suite 400
222 Lakeview Avenue
West Palm Beach, FL 33402-3188

EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
09/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/695,600	STEINDLER ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-32 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-32 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 12, 2007 that includes a response to the final office action dated March 14, 2007, has been entered. Claim 30 has been amended. No claims were cancelled or newly added.

Claims 30-32, and 35-37 remain pending in the application and are under current examination.

Response to Claim Rejections - 35 USC § 112, Written Description

Claims 30-32, and 35-37 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The rejection set forth on p. 3 of the previous office action dated March 14, 2007 is maintained for reasons of record.

Applicants traverse the rejection, arguing that Applicants have described the stem cells and identified the actual markers that identify these stem cells as Type I, II and III cells. Applicants further refer to the description of Figures 1-7 and additionally refer to the descriptions and Examples 1-3 of the specification that "describe the types of purified stem cells". Applicants' arguments have been fully considered, but are not found persuasive.

The instant claims are directed to an *ex vivo* culture of a population of multipotent, progenitor or precursor brain stem cells that are immunonegative for glial fibrillary protein, nestin and TuJ 1. As previously set forth, Applicants have failed to demonstrate possession of any isolated or purified cell types, given that the mixed culture of brain progenitor cells represent a continuum of cell proliferation and differentiation, that is in part dependent upon culture conditions, and further, an Artisan of skill could not differentiate between Type I and early Type II cells, both of which are immunonegative for specific markers. The mixed population of

cultured cells additionally comprises late Type II and Type III cells, clones or spheres, that are immunopositive for glial fibrillary protein, nestin and TuJ 1 markers. Thus, the *ex vivo* culture of a population of multipotent progenitor brain stem cells as instantly claimed comprises different subsets of cells that cannot be simultaneously immunonegative for the aforementioned markers. The instant specification only demonstrates possession of a mixed population of human or mouse brain progenitor cells, comprising Type I, II and III clones.

Hence, the rejection of claims 30-32, and 35-37 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112-Lack of Enablement

Claims 30-32, and 35-37 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The rejection set forth on pp. 3-5 of the previous office action dated March 14, 2007 is maintained for claims, for reasons of record.

Issues regarding the grounds for rejection of the claims pertain to the mixed culture of human and mouse brain progenitor cells, comprising Type I, II and III clones disclosed in the specification and the absence of isolation of any of the progenitor cell subtypes on the basis of cell surface markers.

Applicants disagree with the rejection and reiterate that Applicants have described the stem cells and identified the actual markers that identify these stem cells as Type I, II and III cells, and have provided detailed morphological and phenotypic descriptions, citing Figures 1-7 and the descriptions and Examples 1-3 of the specification that "describe the types of purified stem cells". Applicants additionally argue that because of the high level of skill in the art and the state of the art at the time the application was filed, one of ordinary skill in the art would not have to perform undue experimentation to make and use the invention as claimed. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it is noted that the instant application claims priority to January 7, 1997. As such, the isolation of brain neuroprogenitor or stem cells by a person of ordinary skill in the art at the time of filing was neither routine, nor predictable, as previously indicated by Gage et al. (of

record). Further, as set forth in the previous office action, the instant application's disclosure does not provide an enablement for the isolation of multipotent brain stem cells.

Applicants' specification states: "The different types of clones observed in the cultures described above and in the experiments described below, represent a continuum of cell proliferation and differentiation, with the existence of both early and late type II clones...that eventually differentiate into type III clusters...The potential for numerous, undefined hematopoeitic stem cells still exists...The use of just one feature as an identification tool can occur, although it makes the recognition of the specific stem cell type rather tenuous" (lines 7-17, p. 12). Therefore, the instantly claimed *ex vivo* culture of cells contains type III cells that are not immunonegative for GFAP, nestin and TuJ1.

The instant specification describes the mixed culture of a population of cellular aggregates described as type I, type II and type III (p. 7, lines 16 and 17). The specification describes the dissociation of brain tissue and subsequent propagation of the cells in suspension cultures and concludes: "some type II cells are also present in these cultures" (Example 1, last paragraph). The specification does not describe either the isolation or the purification of a population of cells that are immunonegative for the markers tested (or may be described as type I, in the absence of other cell types). Moreover, it is apparent from the preceding that the culture of brain stem cells contains both type I and type II clones. Type II clones do not attach to either plastic or laminin-coated substrates and become positive for the nestin (p. 8). A definitive test to show isolation of a population of immunonegative type I clones, would require their purification from the mixed culture, and subsequent differentiation into type II and type III clones. Applicants claim a product that is only defined in structure by negative limitations. In the absence of any known positively displayed cell surface markers, the purification of type I clones would require additional experimentation, without any guarantee of success.

In conclusion, the *ex vivo* culture of the mixed population of cell aggregates may not be correctly described as immunonegative for GFAP, nestin TuJ1 markers, because such a definition refers to a subset of the cells present is said mixed culture. Hence, the rejection of claims 30-32 and 35-37 is maintained for reasons of record and the foregoing discussion.

Examiner's Comment

Applicants should note that if the instant claims are amended to recite " a mixed population of *ex vivo* cultured multipotent brain stem cells", the claims may become subject to rejection over the prior art made of record and not relied upon.

Conclusion

Claims 30-32 and 35-37 are not allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633